Notice of Allowability	Application No.	Applicant(s)	
	09/806,368	KATSUURA ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *10/25/2005*.

2. ☒ The allowed claim(s) is/are *24-43*.

3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *200602* .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DAVID S. ROMEO
PRIMARY EXAMINER

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Monica Kitts on January 26, 2006.

The application has been amended as follows:

Listing of Claims:

Claims 1-23 (Canceled)

24. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by replacing at least one methionine or tryptophan residue existing in the receptor binding site of mature human MP52 (SEQ ID NO:1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification.

25. (New) The BMP antagonist according to claim 24, wherein the chemical modification for said tryptophan residue is an allylsulphenylation reaction.

26. (New) The BMP antagonist according to claim 25 in which two tryptophan residues are allylsulphenylated and having the amino acid sequence of SEQ ID NO 7.

27. (New) The BMP antagonist according to claim 24, wherein said mature human MP52 is a dimer protein.

28. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by converting at least one residue of tryptophan residues existing in the amino acid sequences of mature human BMP-2 (SEQ ID NO 2), mature human BMP-4 (SEQ ID NO 3) or mature human BMP-7 (SEQ ID NO 4) to a hydrophilic residue by chemical

modification, or replacing said residues with a hydrophilic amino acid residue or a polar amino acid residue.

29. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by replacing at least one amino acid residue of three hydrophobic amino acid residues, among said hydrophobic amino acid residues relating to a receptor binding site in the amino acid sequences of mature human BMP-2 (SEQ ID NO 2), mature human BMP-4 (SEQ ID NO 3), or mature human BMP-7 (SEQ ID NO 4), which are located in positions corresponding to those of methionine residues located in 30th, 71st, and 74th positions of the amino acid sequence of mature human MP52 (SEQ ID NO 1) with a hydrophilic amino acid residue or a polar amino acid residue.

30. (New) The BMP antagonist according to claim 28, wherein said mature human BMP-2, mature human BMP-4, or mature human BMP-7 is a dimer protein.

31. (New) A therapeutic agent containing a BMP antagonist according to claim 24.

32. (New) A therapeutic agent for therapy of diseases due to the expression of MP52, BMP-2, BMP-4 and/or BMP-7 containing a BMP antagonist according to claim 24 as an effective ingredient.

33. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by converting at least one methionine residue existing in the receptor binding site of mature human MP52 (SEQ ID NO:1) by chemical modification, wherein said chemical modification for said methionine residue is an alkylation reaction.

34. (New) The BMP antagonist according to claim 33, wherein the alkylation reaction is S-carboxymethylation in which at least one methionine residue is S-carboxymethylated and having the amino acid sequence of SEQ ID NO 6.

35. (New) The BMP antagonist according to claim 33, wherein said mature human MP52 is a dimer protein.

36. (New) A therapeutic agent containing a BMP antagonist according to claim 33.

37. (New) A therapeutic agent for therapy of diseases due to the expression of MP52, BMP-2, BMP-4 and/or BMP-7 containing a BMP antagonist according to claim 33 as an effective ingredient.

38. (New) A method for antagonizing MP52, BMP-2, BMP-4 and BMP-7, comprising administering to a patient in need thereof, an effective amount of a mature modified protein according to claim 33.

39. (New) The method according to claim 38, wherein said patient is suffering from ectopic ossification which is due to ectopic expression of MP52, BMP-2, BMP-4 and/or BMP-7.

40. (New) The method according to claim 38, wherein said patient is suffering from a metabolic disease with calcification.

41. (New) The method according to claim 40, wherein said metabolic disease with calcification is calcification of arterial sclerosis.

42. (New) A mature modified protein obtained by replacing at least one methionine residue at position 30, 71 or 74 or at least one tryptophan residue existing in mature human MP52 (SEQ ID NO:1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification, wherein said mature modified protein has antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7.

43. (New) A mature, modified protein obtained by replacing at least one methionine or at least one tryptophan residue existing in the receptor binding site of mature human MP52 (SEQ ID NO 1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification, wherein said mature modified

protein has antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7.

44. (New) A method for antagonizing MP52, BMP-2, BMP-4 and BMP-7, comprising administering to a patient in need thereof, an effective amount of a mature modified protein according to claim 24.

45. (New) The method according to claim 44, wherein said patient is suffering from ectopic ossification which is due to ectopic expression of MP52, BMP-2, BMP-4 and/or BMP-7.

46. (New) The method according to claim 44, wherein said patient is suffering from a metabolic disease with calcification.

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47. (New) The method according to claim ~~47~~ 46, wherein said metabolic disease with calcification is calcification of arterial sclerosis.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
FEBRUARY 6, 2006